News Release

Title
Pioneering axons regulate neuronal polarization in the developing cerebral cortex

Key Points
- Neurons generate axon while in contact with the pioneering axons that express TAG-1.
- TAG-1 is required for axon formation.
- Src family kinase Lyn mediates TAG-1-induced axon formation.

Summary
Prof. Kozo Kaibuchi (Department of Cell Pharmacology) and his team led by Dr. Takashi Namba (Assistant Professor) in Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.) found that cell-to-cell interactions between the early-born neurons and late-born immature neurons induce axon formation of the immature neurons. In this process, cell adhesion molecule named TAG-1 plays critical roles. When TAG-1 was experimentally eliminated from the immature neurons, the axon formation was impaired. These results suggest that the cell-to-cell interaction between the early-born neurons and late-born immature neurons through TAG-1 regulates proper axon formation.

Research Background
Neurons play main roles in the brain function. They receive signals from other neurons and integrate and transmit it to other neurons. To achieve this function, proper axon formation is essential. Studies that have used dissociated neurons from rodent brains have revealed that many kinds of proteins are involved in the establishment of axon. However, how neurons establish their axon in vivo is still unclear. In this study, we focused on the cell-to-cell interactions between the early-born neurons and late-born immature neurons and explored the downstream mechanisms for axon formation.

Research Results
The research group precisely observed the developmental process of axon in vivo. Based on their observation, they found that the immature neurons firstly extend multiple immature neurites and then generate axon. In this process, the neurite that closely contacted with axons from the early-born neurons finally developed into an axon. These results suggest that the cell-to-cell interactions regulate axon formation. Next question is what kinds of molecules regulate this interaction and axon formation. The group focused on TAG-1, a cell adhesion molecule. When TAG-1 was experimentally eliminated from the immature neurons, the axon formation was impaired. Finally, the group identified protein kinase Lyn as a downstream effector of TAG-1. These results suggest that the cell-to-cell interaction between the early-born
neurons and late-born immature neurons through TAG-1 and Lyn regulates proper axon formation.

**Research Summary and Future Perspective**

In summary, this study provides a novel mechanism of axon formation in vivo. Because impairment of the axon formation might correlate directly with the neurodevelopmental disorders, present study will help to understand the etiology of these disorders.


**Japanese ver.**

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